

## SEQUENCE LISTING

<110> INSTITUT PASTEUR  
INSERM (Institut National de la Santé et de la Recherche Médicale)  
CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE  
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COURTOIS, GILLES  
ISRAEL, ALAIN  
VERON, MICHEL  
TRAINCARD, FRANCOIS  
YAMAOKA, SHOJI

<120> SELECTIVE INHIBITION OF NF-Kappab ACTIVATION BY PEPTIDES DESIGNED  
TO DISRUPT NEMO OLIGOMERIZATION

<150> US 60/530,418

<151> 2003-12-18

<150> US 60/505,161

<151> 2003-09-24

<160> 39

<170> PatentIn version 3.3

<210> 1

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<212> PRT

<213> Artificial Sequence

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<223> Synthetic Peptide

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Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
1 5 10 15

Lys

<210> 2

<211> 57

<212> PRT

<213> Artificial Sequence

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Lys Ser Lys Gly Met Gln Leu Glu Asp Leu Arg Gln Gln Leu Gln Gln  
20 25 30

Ala Glu Glu Ala Leu Val Ala Lys Gln Glu Leu Ile Asp Lys Leu Lys  
35 40 45

Glu Glu Ala Glu Gln His Lys Ile Val  
50 55

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Ser Lys Gly Met Gln Leu Glu Asp Leu Arg Gln Gln Leu Gln Gln Ala  
1 5 10 15

Glu Glu Ala Leu Val Ala Lys Gln Glu Leu Ile Asp Lys Leu Lys Glu  
20 25 30

Glu Ala Glu Gln His Lys Ile Val  
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Lys Ser Lys Gly Met Gln Leu Glu Asp Leu Arg Gln Gln Gly Gln Gln  
20 25 30

Ala Glu Glu Ala Gly Val Ala Lys Gln Glu Leu Gly Asp Lys Leu Lys  
35 40 45

Glu Glu Ala Glu Gln His Lys Ile Val  
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Ser Lys Gly Met Gln Leu Glu Asp Leu Arg Gln Gln Gly Gln Gln Ala  
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Glu Glu Ala Gly Val Ala Lys Gln Glu Leu Gly Asp Lys Leu Lys Glu  
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Glu Ala Glu Gln His Lys Ile Val

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Lys Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu  
20                 25                 30

Arg His Ala Arg Glu Lys Leu Val Glu Lys Lys Glu Tyr Leu Gln Glu  
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Gln Leu Glu Gln Leu Gln Arg Glu Phe Asn Lys Leu  
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Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu Arg  
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His Ala Arg Glu Lys Leu Val Glu Lys Lys Glu Tyr Leu Gln Glu Gln  
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Leu Glu Gln Leu Gln Arg Glu Phe Asn Lys Leu  
35                 40

<210> 8  
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<400> 8

Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
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Lys Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu  
20                 25                 30

Arg His Ala Arg Glu Lys Leu Val Glu Lys Lys Glu Tyr Ser Gln Glu  
 35 40 45

Gln Leu Glu Gln Ser Gln Arg Glu Phe Asn Lys Leu  
 50 55 60

<210> 9  
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 <212> PRT  
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<400> 9

Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu Arg  
 1 5 10 15

His Ala Arg Glu Lys Leu Val Glu Lys Lys Glu Tyr Ser Gln Glu Gln  
 20 25 30

Leu Glu Gln Ser Gln Arg Glu Phe Asn Lys Leu  
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Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
 1 5 10 15

Lys Ser Lys Gly Met Gln Arg Met Lys Gln Leu Glu Asp Lys Val Glu  
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Glu Leu Leu Ser Lys Asn Tyr His Leu Glu Asn Glu Val Ala Arg Leu  
 35 40 45

Lys Lys Leu Val Gly Glu Arg  
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&lt;211&gt; 412

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 12

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							20			25			30		

Leu	Gly	Lys	Pro	Ala	Met	Leu	His	Leu	Pro	Ser	Glu	Gln	Gly	Thr	Pro
					35			40				45			

Glu	Thr	Leu	Gln	Arg	Cys	Leu	Glu	Glu	Asn	Gln	Glu	Leu	Arg	Asp	Ala
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Ile	Arg	Gln	Ser	Asn	Gln	Met	Leu	Arg	Glu	Arg	Cys	Glu	Glu	Leu	Leu
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His	Phe	Gln	Val	Ser	Gln	Arg	Glu	Glu	Lys	Glu	Phe	Leu	Met	Cys	Lys
					85			90					95		

Phe Gln Glu Ala Arg Lys Leu Val Glu Arg Leu Ser Leu Glu Lys Leu  
100 105 110

Asp Leu Arg Ser Gln Arg Glu Gln Ala Leu Lys Glu Leu Glu Gln Leu  
115 120 125

Lys Lys Cys Gln Gln Gln Met Ala Glu Asp Lys Ala Ser Val Lys Ala  
130 135 140

Gln Val Thr Ser Leu Leu Gly Glu Leu Gln Glu Ser Gln Ser Arg Leu  
145 150 155 160

Glu Ala Ala Thr Lys Asp Arg Gln Ala Leu Glu Gly Arg Ile Arg Ala  
165 170 175

Val Ser Glu Gln Val Arg Gln Leu Glu Ser Glu Arg Glu Val Leu Gln  
180 185 190

Gln Gln His Ser Val Gln Val Asp Gln Leu Arg Met Gln Asn Gln Ser  
195 200 205

Val Glu Ala Ala Leu Arg Met Glu Arg Gln Ala Ala Ser Glu Glu Lys  
210 215 220

Arg Lys Leu Ala Gln Leu Gln Ala Ala Tyr His Gln Leu Phe Gln Asp  
225 230 235 240

Tyr Asp Ser His Ile Lys Ser Ser Lys Gly Met Gln Leu Glu Asp Leu  
245 250 255

Arg Gln Gln Leu Gln Gln Ala Glu Glu Ala Leu Val Ala Lys Gln Glu  
260 265 270

Leu Ile Asp Lys Leu Lys Glu Glu Ala Glu Gln His Lys Ile Val Met  
275 280 285

Glu Thr Val Pro Val Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp  
290 295 300

Phe Gln Ala Glu Arg His Ala Arg Glu Lys Leu Val Glu Lys Lys Glu  
305 310 315 320

Tyr Leu Gln Glu Gln Leu Glu Gln Leu Gln Arg Glu Phe Asn Lys Leu  
325 330 335

Lys Val Gly Cys His Glu Ser Ala Arg Ile Glu Asp Met Arg Lys Arg  
340 345 350

His Val Glu Thr Pro Gln Pro Pro Leu Leu Pro Ala Pro Ala His His  
355 360 365

Ser Phe His Leu Ala Leu Ser Asn Gln Arg Arg Ser Pro Pro Glu Glu  
370 375 380

Pro Pro Asp Phe Cys Cys Pro Lys Cys Gln Tyr Gln Ala Pro Asp Met  
385 390 395 400

Asp Thr Leu Gln Ile His Val Met Glu Cys Ile Glu  
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<210> 13

<211> 57

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Peptide

<400> 13

Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
1 5 10 15

Lys Ser Lys Gly Met Gln Leu Glu Asp Leu Lys Gln Gln Leu Gln Gln  
20 25 30

Ala Glu Glu Ala Leu Val Ala Lys Gln Glu Val Ile Asp Lys Leu Lys  
35 40 45

Glu Glu Ala Glu Gln His Lys Ile Val  
50 55

<210> 14

<211> 40

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Peptide

<400> 14

Ser Lys Gly Met Gln Leu Glu Asp Leu Lys Gln Gln Leu Gln Gln Ala  
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Glu Glu Ala Leu Val Ala Lys Gln Glu Val Ile Asp Lys Leu Lys Glu  
20 25 30

Glu Ala Glu Gln His Lys Ile Val  
35 40

<210> 15

<211> 60

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Peptide

<400> 15

Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
1 5 10 15

Lys Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu  
20 25 30

Arg Gln Ala Arg Glu Lys Leu Ala Glu Lys Lys Glu Leu Leu Gln Glu  
35 40 45

Gln Leu Glu Gln Leu Gln Arg Glu Tyr Ser Lys Leu  
50 55 60

<210> 16

<211> 43

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Peptide

<400> 16

Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu Arg  
1 5 10 15

Gln Ala Arg Glu Lys Leu Ala Glu Lys Lys Glu Leu Leu Gln Glu Gln  
20 25 30

Leu Glu Gln Leu Gln Arg Glu Tyr Ser Lys Leu  
35 40

<210> 17

<211> 2035

<212> DNA

<213> Homo sapiens

<400> 17

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<210> 18  
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<400> 18

Met Asn Arg His Leu Trp Lys Ser Gln Leu Cys Glu Met Val Gln Pro  
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Ser Gly Gly Pro Ala Ala Asp Gln Asp Val Leu Gly Glu Glu Ser Pro  
20 25 30

Leu Gly Lys Pro Ala Met Leu His Leu Pro Ser Glu Gln Gly Ala Pro  
35 40 45

Glu Thr Leu Gln Arg Cys Leu Glu Glu Asn Gln Glu Leu Arg Asp Ala  
Page 9

50	55	60
Ile Arg Gln Ser Asn Gln Ile Leu Arg Glu Arg Cys Glu Glu Leu Leu		
65	70	75
His Phe Gln Ala Ser Gln Arg Glu Glu Lys Glu Phe Leu Met Cys Lys		
85	90	95
Phe Gln Glu Ala Arg Lys Leu Val Glu Arg Leu Gly Leu Glu Lys Leu		
100	105	110
Asp Leu Lys Arg Gln Lys Glu Gln Ala Leu Arg Glu Val Glu His Leu		
115	120	125
Lys Arg Cys Gln Gln Gln Met Ala Glu Asp Lys Ala Ser Val Lys Ala		
130	135	140
Gln Val Thr Ser Leu Leu Gly Glu Leu Gln Glu Ser Gln Ser Arg Leu		
145	150	155
160		
Glu Ala Ala Thr Lys Glu Cys Gln Ala Leu Glu Gly Arg Ala Arg Ala		
165	170	175
Ala Ser Glu Gln Ala Arg Gln Leu Glu Ser Glu Arg Glu Ala Leu Gln		
180	185	190
Gln Gln His Ser Val Gln Val Asp Gln Leu Arg Met Gln Gly Gln Ser		
195	200	205
Val Glu Ala Ala Leu Arg Met Glu Arg Gln Ala Ala Ser Glu Glu Lys		
210	215	220
Arg Lys Leu Ala Gln Leu Gln Val Ala Tyr His Gln Leu Phe Gln Glu		
225	230	235
240		
Tyr Asp Asn His Ile Lys Ser Ser Val Val Gly Ser Glu Arg Lys Arg		
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Gly Met Gln Leu Glu Asp Leu Lys Gln Gln Leu Gln Gln Ala Glu Glu		
260	265	270
Ala Leu Val Ala Lys Gln Glu Val Ile Asp Lys Leu Lys Glu Glu Ala		
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Glu Gln His Lys Ile Val Met Glu Thr Val Pro Val Leu Lys Ala Gln		
290	295	300
Ala Asp Ile Tyr Lys Ala Asp Phe Gln Ala Glu Arg Gln Ala Arg Glu		
305	310	315
320		
Lys Leu Ala Glu Lys Lys Glu Leu Leu Gln Glu Gln Leu Glu Gln Leu		

325

330

335

Gln Arg Glu Tyr Ser Lys Leu Lys Ala Ser Cys Gln Glu Ser Ala Arg  
 340 345 350

Ile Glu Asp Met Arg Lys Arg His Val Glu Val Ser Gln Ala Pro Leu  
 355 360 365

Pro Pro Ala Pro Ala Tyr Leu Ser Ser Pro Leu Ala Leu Pro Ser Gln  
 370 375 380

Arg Arg Ser Pro Pro Glu Glu Pro Pro Asp Phe Cys Cys Pro Lys Cys  
 385 390 395 400

Gln Tyr Gln Ala Pro Asp Met Asp Thr Leu Gln Ile His Val Met Glu  
 405 410 415

Cys Ile Glu

<210> 19  
 <211> 51  
 <212> PRT  
 <213> Mus musculus

<400> 19

Glu Leu Ile Asp Lys Leu Lys Glu Glu Ala Glu Gln His Lys Ile Val  
 1 5 10 15

Met Glu Thr Val Pro Val Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala  
 20 25 30

Asp Phe Gln Ala Glu Arg His Ala Arg Glu Lys Leu Val Glu Lys Lys  
 35 40 45

Glu Tyr Leu  
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<210> 20  
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 <213> Homo sapiens

<400> 20

Glu Val Ile Asp Lys Leu Lys Glu Glu Ala Glu Gln His Lys Ile Val  
 1 5 10 15

Met Glu Thr Val Pro Val Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala  
 20 25 30

Asp Phe Gln Ala Glu Arg Gln Ala Arg Glu Lys Leu Ala Glu Lys Lys  
 35 40 45

Glu Leu Leu  
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<210> 21  
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<213> Bos taurus

<400> 21

Glu Val Ile Asp Lys Leu Lys Glu Glu Ala Glu Gln His Lys Ile Val  
1 5 10 15

Met Glu Thr Val Pro Val Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala  
20 25 30

Asp Phe Gln Ala Glu Arg Gln Ala Arg Glu Lys Leu Ala Glu Lys Lys  
35 40 45

Glu Phe Leu  
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<210> 22  
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<213> Drosophila melanogaster

<400> 22

Glu Leu Ile Lys Lys Met Gln Leu Asp Ile Asn Glu Leu Lys Ala Arg  
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Asp Ile Gln Lys Gln Glu Val Ile Lys Gly Leu Gln Ile Gln Asn Asp  
20 25 30

Ile Tyr Arg Arg Asp Phe Glu Met Glu Arg Ala Asp Arg Glu Lys Asn  
35 40 45

Ala Gly Glu Lys Asp Gln Tyr  
50 55

<210> 23  
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<212> PRT  
<213> Mus musculus

<400> 23

Leu Gln Met Asp Glu Met Lys Gln Thr Leu Ala Lys Gln Glu Glu Asp  
1 5 10 15

Leu Glu Thr Met Ala Val Leu Arg Ala Gln Met Glu Val Tyr Cys Ser  
20 25 30

Asp Phe His Ala Glu Arg Ala Ala Arg Glu Lys Ile His Glu Glu Lys  
35 40 45

Glu Gln Leu  
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<210> 24  
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<213> Homo sapiens  
  
<400> 24

Leu Gln Met Asp Glu Met Lys Gln Thr Ile Ala Lys Gln Glu Glu Asp  
1 5 10 15

Leu Glu Thr Met Thr Ile Leu Arg Ala Gln Met Glu Val Tyr Cys Ser  
20 25 30

Asp Phe His Ala Glu Arg Ala Ala Arg Glu Lys Ile His Glu Glu Lys  
35 40 45

Glu Gln Leu  
50

<210> 25  
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<400> 25

Ser Pro Ser Ser Pro Pro Ala Ala Phe Gly Ser Pro Glu Gly Val Gly  
1 5 10 15

Gly His Leu Arg Lys Gln Glu Leu Val Thr Gln Asn Glu Leu Leu Lys  
20 25 30

Gln Gln Val Lys Ile Phe Glu Glu Asp Phe Gln Arg Glu Arg Ser Asp  
35 40 45

Arg Glu Arg Met Asn Glu Glu Lys Glu Glu Leu  
50 55

<210> 26  
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<213> Homo sapiens  
  
<400> 26

Pro Pro Ser Ser Pro Pro Thr Ala Phe Gly Ser Pro Glu Gly Ala Gly  
1 5 10 15

Ala Leu Leu Arg Lys Gln Glu Leu Val Thr Gln Asn Glu Leu Leu Lys  
20 25 30

Gln Gln Val Lys Ile Phe Glu Glu Asp Phe Gln Arg Glu Arg Ser Asp  
Page 13

35

40

45

Arg Glu Arg Met Asn Glu Glu Lys Glu Glu Leu  
50 55

<210> 27  
<211> 51  
<212> PRT  
<213> Mus musculus

<400> 27

Glu Ala Asn Gln Glu Leu Thr Ala Met Arg Met Ser Arg Asp Thr Ala  
1 5 10 15

Leu Glu Arg Val Gln Met Leu Glu Gln Gln Ile Leu Ala Tyr Lys Asp  
20 25 30

Asp Phe Lys Ser Glu Arg Ala Asp Arg Glu Arg Ala His Ser Arg Ile  
35 40 45

Gln Glu Leu  
50

<210> 28  
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<212> PRT  
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<400> 28

Glu Val Lys Gln Glu Leu Ala Ala Ser Arg Thr Ala Arg Asp Ala Ala  
1 5 10 15

Leu Glu Arg Val Gln Met Leu Glu Gln Gln Ile Leu Ala Tyr Lys Asp  
20 25 30

Asp Phe Met Ser Glu Arg Ala Asp Arg Glu Arg Ala Gln Ser Arg Ile  
35 40 45

Gln Glu Leu  
50

<210> 29  
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<212> PRT  
<213> Homo sapiens

<400> 29

Ser Phe Ser Glu Asp Cys Leu Arg Lys Ser Arg Val Glu Phe Cys His  
1 5 10 15

Glu Glu Met Arg Thr Glu Met Glu Val Leu Lys Gln Gln Val Gln Ile  
20 25 30

Tyr Glu Glu Asp Phe Lys Lys Glu Arg Ser Asp Arg Glu Arg Leu Asn  
35 40 45

Gln Glu Lys Glu Glu Leu  
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<210> 30  
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Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu Arg  
1 5 10 15

His Ala Arg Glu Lys  
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<210> 31  
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<212> PRT  
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Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
1 5 10 15

Lys Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu  
20 25 30

Arg His Ala Arg Glu Lys  
35

<210> 32  
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<212> PRT  
<213> Artificial Sequence

<220>  
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<400> 32

Cys Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg Leu Lys Ala Gln  
1 5 10 15

Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu Arg His Ala Arg Glu  
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Lys

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Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu Arg  
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Gln Ala Arg Glu Lys  
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Cys Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys  
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Lys Leu Lys Ala Gln Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu  
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Arg Gln Ala Arg Glu Lys  
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Cys Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg Leu Lys Ala Gln  
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Ala Asp Ile Tyr Lys Ala Arg Phe Gln Ala Glu Arg Gln Ala Arg Glu  
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Lys

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Cys Arg Arg Arg Arg Arg Arg Leu Lys Ala Gln Ala Asp Ile Tyr  
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Lys Ala Arg Phe Gln Ala Glu Arg Gln Ala Arg Glu Lys  
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Cys Arg Arg Arg Arg Arg Arg Arg Leu Lys Ala Gln Ala Asp  
1 5 10 15

Ile Tyr Lys Ala Arg Phe Gln Ala Glu Arg Gln Ala Arg Glu Lys  
20 25 30